On the Nonlinear Relation between BOLD and CBF

T.T. Liu[1], W.-M. Luh[1], E.C. Wong[1,2], P.A. Bandettini[3], T. Obata[1], L.R. Frank[1], R.B. Buxton[1]
[1]Depts. of Radiology and [2]Psychiatry, University of California, San Diego
and [3]Laboratory of Brain and Cognition, NIMH

Introduction: Although models of BOLD signal change predict a non-linear relation between the percent change in BOLD and the percent change in CBF [1,2], there is some evidence of a linear correlation between BOLD and CBF [3]. If a nonlinearity exists, it should become more apparent with the application of diffusion weighting [2]. In this abstract we present measurements, with and without diffusion weighting, of BOLD and CBF increases in primary motor cortex. The data show good agreement with a nonlinear model.

Theory: We use a BOLD signal model [1,4] of the form

$$\frac{\Delta S}{S} = V_0\left[(k_1+k_2)(1-q)-(k2+k3)(1-v)\right],$$

where V_0 is the resting blood volume fraction, and q and v are the normalized total deoxyhemoglobin content and blood volume, respectively. The dimensionless parameters are $k_1 = 4.3\nu_0 E_0 TE$, $k_2 = \xi r_0 E_0 TE$, and $k_3 = \xi - 1$. E_0 is the resting oxygen extraction fraction and $\nu_0 = 80.6$ Hz at 3T. ξ is the ratio of the intravascular (IV) to extravascular (EV) components, and assuming equal EV and IV proton densities, is $exp((-R^*_{2,IV} + R^*_{2,EV})TE)$. We assume a linear form $R^*_{2,IV} = \alpha + r_0 E$ for the IV relaxation rate over the range of extraction fraction E (roughly 0.2 to 0.4) that is typically encountered [5]. With linear coupling between percent increases in oxygen metabolism rate and blood flow, the extraction fraction has the form $E(f) = E_0(f-1+n)/(nf)$, where f is CBF normalized to its resting value and n is the ratio of the fractional changes in CBF and $CMRO_2$. We assume that volume follows the relation $v = f^{0.38}$ [6]. To approximate the effects of diffusion weighting, we multiply ξ by an attenuation factor β_0, where $0 \le \beta_0 \le 1$. We assume $E_0 = 0.4$, $\alpha = 5\ s^{-1}$, $n = 6$, and treat V_0, β_0 and r_0 as free parameters to be determined by a model fit to the data. $R^*_{2,EV}$ is estimated from the ratio of the first and second echos (see Methods), and in conjunction with α and r_0 constrains the value of ξ.

Methods: Subjects (n=3) performed bilateral sequential finger tapping paced by a flashing LED display (GRASS goggles). Two flash rates were used: a slow 1 Hz rate (subjects tapped once per second) and a fast 8 Hz rate (subjects tapped as rapidly as possible). Each run consisted of a 16s off period followed by 8 cycles of 20s on, 40s off. Four runs at each flash rate were acquired. Imaging was performed on a 3T GE Signa LX system. Two contiguous oblique slices (FOV=24cm, slice thickness=4mm, matrix=64x64) cutting through the primary motor cortex were imaged. PICORE QUIPPS II [7] was used for arterial spin tagging with a 10 cm tagging band and $TI_1 = 700$ms, $TI_2 = 1400$ms, $TR = 2$s. Readout was performed with a double echo spiral pulse sequence ($TE_1 = 2.7$ms, $TE_2 = 43$ms) with a bipolar gradient pulse (4 G/cm, 19.6 ms total duration, venc=0.3 cm/s, b=66.3 s/mm^2) inserted between the two spirals. Diffusion weighting was applied every other tag-control pair.

Flow and BOLD time series were formed from the difference/sum of the control and tag images acquired with the first/second echo, respectively. Images were coregistered, and a fourth-order polynomial was removed from each pixel time course. BOLD data were divided into diffusion weighted and non-diffusion weighted time series. The data were then averaged over four runs (fast or slow tapping) and collapsed over cycles to form a 1 cycle long time series. Correlation of the flow time series (fast tapping paradigm) with a boxcar reference function (threshold = 0.5) and a clustering algorithm (at least two nearest neighbors) were used to select activated voxels. All activated voxels within the primary motor cortex region were averaged to form an average flow and BOLD time series.

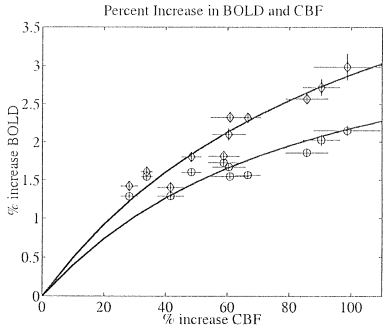

Figure 1: Percent increase in BOLD vs. CBF in primary motor cortex, with (circles) and without (diamonds) diffusion weighting. Model fit is shown by solid lines. Bars indicate standard errors.

Results: Figure 1 shows the average percent increases in BOLD (with and without diffusion weighting) versus the average percent increases in CBF. Each data point corresponds to the average from one slice in one subject for a given speed of finger tapping. A nonlinear optimization algorithm was used to determine the parameters ($V_0 = 0.018$, $\beta_0 = 0.13$, $r_0 = 90$ Hz) that minimized the mean-squared error between the BOLD signal model and the data. The algorithm was run with the constraints: $V_0 > 0$, $0 < r_0 \le 90$, and $0 \le \beta_0 \le 1$. The resulting model fit is shown in Figure 1. The root mean squared error of the fit is 0.24 percent.

Conclusion: The nonlinear BOLD signal model provides a good fit to the data over a wide range of CBF percent increases. Over limited ranges of CBF increases, the data exhibit an approximately linear relation between BOLD and CBF percent increases. This finding is consistent with the fact that previous reports of a linear relation [3] were obtained over a small range of CBF percent increases.

References: [1] Buxton, R.B. et al. MRM 39:855, 1998. [2] Boxerman, J.L. et al. MRM 34:4, 1995. [3] Zhu, X.-H. et al. MRM 40:703, 1998. [4] Buxton, R.B. et al. Proc. ISMRM, p. 1735, 1999. [5] Li, D.B. et al. MRM 30:683, 1998. [6] Grubb, R. et al. Stroke 5:360, 1974. [7] Wong, E.C. et al. MRM 39:702, 1998.

Acknowledgments: Thanks to Gary Glover for the basic spiral pulse sequence upon which this was built.